POLYNEURITIS ASSOCIATED WITH VOMITING OF PREGNANCY *

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POLYNEURITIS, following the vomiting of pregnancy, is of special interest since it is associated with faulty metabolism and changes in the nervous system, some of which are irreversible. The preponderance of evidence indicates that the cause of this syndrome is either an inadequate ingestion of vitamins or the inability to metabolize these substances properly, even though they be present in the diet. Polyneuritis might be prevented during pregnancy by the administration of prophylactic diets; and even when the disease manifests itself, improvement may be anticipated by the use of a high vitamin intake.

It is noteworthy that the first case of polyneuritis associated with psychosis reported by Korsakoff [1] developed after pregnancy. Whitfield,[2] von Hösslin,[3] Ely,[4] Albeck,[5] Hofmann,[6] Weill-Hallé and Layani,[7] Ledoux,[8] Dupouy and Courtois,[9] and Berkwitz and Lufkin,[10] concluded that polyneuritis associated with pregnancy is frequently related to hyperemesis gravidarum.

POLYNEURITIS AND DIET DEFICIENCIES

Interest in the interrelationship of polyneuritis of all types and dietary deficiencies was greatly stimulated by Wechsler,[11] who published a preliminary report on this subject in 1930. In a more recent publication, Wechsler [12] reports five cases of polyneuritis in which the diagnosis and the decisive etiologic factors are given. One of these cases followed vomiting of pregnancy and showed the typical findings consistent with the diagnosis, as well as a remarkable and rapid improvement after the administration of a full diet, rich in vitamins. Strauss and McDonald [13] report three similar cases and state that: "(1) The polyneuritis of pregnancy is probably a dietary deficiency disorder similar to beriberi. (2) Rational therapy should aim to supply the deficiency, which may be especially some portion of the vitamin B complex; large amounts of concentrates of this substance are advised."

REPORT OF CASE

The following case, similar to those of Wechsler and Strauss and McDonald, is reported:

Mrs. R. H. A., American, age 22 years, was admitted to Mary's Help Hospital, San Francisco, on December 5, 1932, complaining of inability to use her legs (duration, four days), a "dead feeling" below the waist (duration, four days), and painful sensations throughout the upper abdomen (duration, three days).

The family history and past history are essentially irrelevant, there being no history of exposure to exogenous toxins or the habitual use of alcohol. The patient states that she was perfectly well until the middle of August, 1932, (three and one-half months before entrance into the hospital), at which time she became pregnant. The pregnancy was characterized by almost continuous vomiting and a loss of thirty pounds in body weight. Two and one-half weeks before entrance the patient aborted spontaneously. Following the termination of her pregnancy the vomiting became less frequent, and the patient began to take food fairly regularly for the first time since the onset of her pregnancy. There were no untoward symptoms until four days before she was admitted to the hospital.

Physical examination on admission: The patient was a rather dulled, moderately intelligent young woman, definitely overweight. She did not appear to be acutely ill. The cardiorespiratory, genito-urinary, and gastro-intestinal systems revealed nothing pathological except for generalized tenderness without rigidity of the upper half of the abdomen.

The essential positive findings of the neurologic examination at this time were:

1. Definite blurring of the optic disks;
2. Markedly diminished power in both arms;
3. Complete absence of all deep and superficial reflexes;
4. Patchy areas of anesthesia and analgesia over both legs and thighs. (The patient was able to perceive touch and pain in many isolated spots between the anesthetic areas);
5. Vibratory and deep-joint sensibilities were absent over the malleoli;
6. Flaccid paralysis of both lower extremities, except that the patient was able to dorsiflex her toes slightly.

The temperature on admission was 100, the pulse 120, and the respiration 22. The urine was negative except for a slight trace of albumin. The blood examination revealed an erythrocyte count of 3.25 millions, hemoglobin of 65 per cent, and 10,600 leukocytes with 76 per cent polymorphonuclears.

On December 8 a spinal puncture was done, the results of which were normal in all respects. The fluid was clear and under normal pressure. The Queckenstedt maneuver was negative. The total protein was 12 milligrams per 100 cubic centimeters. The cell count revealed two lymphocytes, and the stained centrifuged specimen disclosed no organisms.

On December 10 the patient was seen by various members of the hospital staff, and additional findings of vertical and horizontal nystagmus, as well as absence of rectal sphincter tone were noted. On December 11 her arms were observed to be very weak, and for several hours she complained of partial blindness and inability to swallow. A second lumbar puncture was done with similar negative results. The following day she complained of numbness of the left hand, particularly about the tips of the fingers. She suffered from marked dyspnea. The disk margins were still blurred.

On December 14 the patient was considerably more toxic. She was slightly cyanotic, and her respirations were irregular and labored. Because of the severe dyspnea it was necessary to administer oxygen inhalations periodically. There was both rectal and urinary incontinence, and the patient complained of paresthesia and weakness of the hands. The patient was mentally confused, extremely irritable, and had a tendency to confabulate.

Twelve days later a third spinal puncture was done. This likewise showed no evidence of disease. At this time the patient was complaining of pain in her legs as well as numbness and weakness of both hands. On January 9 the patient's general condition had improved. The dyspnea and cyanosis had practically disappeared, and there was partial return of power in her legs. The hands showed considerable atrophy of the small muscles. A fourth lumbar puncture, done at this time, was also negative.

The patient, from this time on, began to show gradual improvement. She regained partial control

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of both sphincters before February 1. The sensory disturbances of her lower extremities gradually diminished. The tenderness of the peripheral nerves still persisted, as well as the atrophy and weakness of the hands. Her temperature returned to normal except for an occasional rise to 99 degrees.

The treatment while in Mary's Help Hospital consisted of bed rest and a high caloric diet, which included the daily ingestion of eight ounces of orange or tomato juice, nine teaspoonsful of Vitavose, and three capsules of Haliver Oil. Physiotherapy, in the form of dry heat was used throughout her stay in the hospital, and from time to time splints were applied to her extremities. On March 8 the patient was transferred to the University of California Medical Service at the San Francisco Hospital.

At that time the physical examination revealed a poorly coöperating, mentally sluggish young woman. The hands and feet were in casts. There was occasional rectal and urinary incontinence. The memory was poor for recent events, and there were evidences of a psychosis of the Korsakoff type. There was persistent lateral nystagmus and bilateral optic neuritis. The gums bled freely and the tongue was smooth. The cardiorespiratory and gastro-intestinal systems revealed nothing abnormal.

After removal of the casts it was noted that, besides a flaccid paralysis of all extremities, there was hyperextension of the metacarpophalangeal joints associated with marked atrophy of the thenar, hypothenar, and interosseous spaces. The patient was unable to move any joint below the elbows. The feet were immobile and edematous, and the legs were markedly wasted. The deep reflexes were unobtainable. Because of the hyperesthesiae, the Babinski and Oppenheim meneuvers could not be elicited. Examination of the blood resulted in normal findings. The blood serum Wassermann reaction was negative. A barium enema revealed no abnormality. The alcohol test-meal provoked a maximum response of 12 degrees of free hydrochloric acid after forty-five minutes.

For the next sixteen days the clinical course was rather turbulent. The patient remained uncoöperative. The temperature varied between 99 and 102 degrees Fahrenheit, the pulse between 90 and 130 per minute, and occasional attacks of dyspnea were noted.

On March 25 the fever subsided and the patient no longer had urinary incontinence. She was able to move her hands slightly. She complained of abdominal pain. One week later, control of the rectal sphincter was regained.

On April 23 she had recovered sufficient use of her hands to enable her to hold a cup, spoon, and fork. From then on she began to feed herself. Movements of the toes and feet became perceptible, and occasionally the patellar reflexes could be obtained. Improvement was slow but steady. The patient gradually acquired some power in the hands; the muscle atrophy, however, persisting unchanged. The patient for the first time was mentally alert, coöperative, and well oriented.

On May 18 the patient was able to support her body weight on her feet for the first time since the onset of the illness. There was still some edema of the feet and ankles. One week later she was able to walk, using chairs and other fixed objects for support. On June 8 a leukocytosis of 15,200 was noted, with 48 per cent polymorphonuclears and 40 per cent lymphocytes.

On June 12, the day of discharge, the patient was free from all subjective complaints. The margins of the right optic disk were still indistinct, and fine lateral nystagmoid movements were present in this eye. Although the patient was able to walk with support, she still had a bilateral foot-drop, more marked on the right. The legs below the knees were cyanotic and cold, and there was excessive perspiration of the feet. There was atrophy of the small muscles of the hands, particularly around the thenar and hypothenar eminences, and some atrophy on the medial surfaces of both thighs, more marked on the right. The patient was unable to use the flexors and extensors of the ankles. There was marked tenderness on deep palpation over the posterior tibial nerves. All four extremities were flaccid. The deep reflexes were present, but very sluggish. The abdominal reflexes could not be obtained. The Babinski maneuver could still not be elicited because even gentle stimulation of the soles produced excruciating pain. The sensation to light touch was markedly diminished over the tips of the fingers and middle phalanges of both hands. The same regions were also hypo-algesic. There was almost complete absence of epicritic sensation associated with hypo-algesia over both feet, ankles, and lower third of the tibiae. Deep joint sensibility was absent in both great toes. Vibratory sensibility was impaired particularly over the bony prominences of the feet, especially the left.

During her stay in the hospital the patient was given symptomatic treatment in conjunction with a high vitamin diet, yeast, cod-liver oil, and dilute hydrochloric acid.

COMMENT

It is noteworthy that polyneuritis, from whatever cause, has been found to be almost invariably associated with a greatly reduced or even complete absence of free hydrochloric acid in the gastric juice. It is probable that the avitaminosis may be due not only to a lack of ingestion of food, but also to the inability to digest, assimilate, or metabolize it. Quite possibly the presence of the fetus in utero may, in some way, disturb these processes so that polyneuritis may occasionally be encountered in pregnancies, during the course of which little vomiting occurs. Wechsler comments upon the fact that in many cases of polyneuritis, other than those associated with pregnancy, in which the condition is supposed to be due to some exogenous poison such as alcohol, lead, arsenic, or phosphorus, it is usual to find the additional factor of avitaminosis. These toxic substances have a tendency to affect the gastric mucosa, the liver, or both, and very probably interfere with the normal absorption of foods. This conception explains very well why polyneuritis develops in only certain persons, although many are exposed to the same poison.

It is generally conceded that the pathologic changes associated with peripheral neuritis, no matter what the cause, are degenerative rather than inflammatory, and usually involve not only the peripheral nervous system, but the anterior horn cells, as well as some of the motor and sensory tracts in the spinal cord. This is adequately shown in connection with the changes in the central nervous system so frequently associated with pernicious anemia, pellagra, and diabetes.[14,15]

Although the antineuritic vitamins B_1, B_2 or G, are involved in connection with beriberi and pellagra, no definite evidence has been brought to light to prove conclusively which of the several vitamins is concerned with the more obscure syndromes. There is some experimental evidence to indicate that the absence of vitamin A, and also possibly vitamins C and D, frequently leads to degenerative changes in the spinal cord, the spinal roots, and the peripheral nerves. Probably in the absence of one or several of these vitamins, the presence of some toxin tends to bring about degenerative changes in the nervous system.

SUMMARY AND CONCLUSIONS

1. A case of polyneuritis associated with hyperemesis of pregnancy is reported. This patient showed marked improvement following the administration of a vitamin-rich diet.

2. The pathogenesis of the syndrome of polyneuritis associated with pregnancy is:

(*a*) Hyperemesis, which produces virtual starvation, thereby depriving the patient of all essential food elements, including the vitamins.

(*b*) Even in the absence of hyperemesis, the presence of the fetus may conceivably alter the maternal metabolism so as to prevent the adequate absorption of the vitamins which are included in the diet. This may be the case even when these food elements are present in amounts sufficient to prevent the development of polyneuritis in the nonpregnant woman. In other words, it is possible that the presence of the fetus may, in susceptible women, act analogously to an exogenous poison such as lead, arsenic or alcohol in the nonpregnant individual, by decreasing the capacity for normal vitamin metabolism.

At least two of the well-defined toxemias of pregnancy exert their chief effect upon the liver, namely, acute yellow atrophy and eclampsia, so that it is not unreasonable to suppose that the development of polyneuritis in pregnancy may also be due to hepatic dysfunction, inasmuch as it is well recognized that the liver bears the brunt of the changes in maternal metabolism created by pregnancy.

3. It is advised that the diet throughout pregnancy be routinely reinforced with vitamin-rich substances. This easily applied precaution should be quite as much a part of the systematic prenatal care as the strict attention invariably paid to the teeth, blood pressure, urine, etc.

In most cases this prophylactic regimen should be effective in preventing the development of polyneuritis. Should the pregnancy, however, be complicated by excessive vomiting, the potential menace of polyneuritis becomes increasingly ominous, and it is obvious that under such conditions the persistent administration of a superabundance of vitamins becomes an urgent necessity.

4. For the actual treatment of polyneuritis, the prompt and continued administration of a diet fortified with all the vitamins constitutes the most logical and hopeful form of therapy.

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DISCUSSION

H. Douglas Eaton, M. D. (1136 West Sixth Street, Los Angeles).—The suggestion that food deficiencies bear a causal relationship to degenerative diseases of the nervous system has been made with increasing frequency in the last few years. In reviewing the cases belonging in this group that have been seen by the writer during the last ten years, it was noted that practically all of them showed degrees of malnutrition varying from severe to extreme. The majority gave a history of dietary deficiencies, and many had a record of marked gastro-intestinal symptoms with or without pathology. These facts are in keeping, of course, with the food deficiency factor theory.

Whether the food deficiency, or so-called avitaminosis, is the sole cause has not been conclusively proved. The clinical records of many of these cases, as well as some experimental work, indicate the existence of a toxemia possibly of hepatic origin. Which is cart and which is horse is not altogether clear.

Further knowledge on this subject will come from just such excellent case reports and observations as are contained in the article of Doctors Gerstle and Lucia. As our knowledge of the vitamins increases, more light will undoubtedly be shed on this interesting and important question.

The theory suggested seems adequate to explain the genesis of the case under discussion. Absolute proof must await further data. Certainly, the author's suggestions as to prevention will prove of definite value.

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Karl L. Schaupp, M. D. (490 Post Street, San Francisco).—In discussing this paper there is the temptation to relate in detail the story of the only case of polyneuritis associated with the vomiting of pregnancy that has come to our attention. This would make a paper of equal or greater length, with no added information other than that secured from the pathologist's report after autopsy.

Our patient at the San Francisco Hospital was a Greek woman of thirty-three years. Except for influenza, she had always been well. She had had one child, five years before, and had had a perfectly normal prenatal period. The present pregnancy commenced about August 1, 1932. Nausea began after one month, and continued until admission three weeks later, or September 22.

On admission, nothing abnormal was noted except that the patient was dehydrated, and that she would cause herself to vomit by inserting a finger into her throat and by coughing.

Treatment consisted in the usual measures for mild cases of hyperemesis, and she responded so well that she was dismissed from the hospital in eight days after having been free from nausea for three days. She was eating well, and said that she was "feeling fine." On October 23 she reëntered the hospital and complained of vomiting again.

Physical Examination.—Revealed a rather well developed but poorly nourished female, who was disinterested in her surroundings and welfare. Head, neck, lungs, and heart, all negative. Abdominal examination negative, except for a firm uterus lying in the midline about 14 centimeters above symphysis. Pelvic examination showed a hard, small, blue cervix, but was otherwise negative. Remainder of physical examination negative. Blood pressure, 120/80.

Laboratory Tests.—Urine: negative. Blood: hemoglobin, 92 per cent; red blood cells, 4,500,000; white blood cells, 6,050; polymorphonuclears, 76 per cent; lymphocytes, 24 per cent. Wassermann: negative.

Course in Hospital.—During her stay in the hospital the patient's condition became progressively worse. She refused to eat, and when she did, vomiting resulted in practically every instance. Saline and glucose instillations were given, but she soon refused them. Gavage was tried with no success.

About November 25, she started to complain of spots before the eyes, double vision and dimness of vision. The eye-grounds showed several small hemorrhages. Urine gave rather strong acetone reaction, but was otherwise negative. Blood pressure as before, 120/80.

Further Laboratory Procedures

CO_2 combining power, 49.

Urine remained negative, except for acetone.

Blood pressure remained 120/80.

Pulse fluctuated around 110 and temperature remained normal.

Dr. Julian Wolfsohn saw the patient on about December 13, and made the following note:

"No hallucinations; tends to drop into stupor. Shows evidence of pain on manipulation. Spontaneous nystagmus when moving eyes to either side.

"Cranial Nerves.—Small pupils which react to light; several fresh and old hemorrhages in both retinae; marked rotary lateral nystagmus in both directions; no ptosis.

"Deep Reflexes.—Biceps, triceps and radial, active and equal. Knee and ankle jerk absent; Babinski negative. No evidence of muscle paralysis. Marked tenderness on pressure over posterior tibialis and muscles in general. Skin of legs dry and crusted. Brudzinski and Kernig negative.

"Diagnosis.—In view of positive findings, this is a case of multiple peripheral neuritis; or, better still, neuronitis affecting the brain and peripheral nerves. Most probably due to some toxin associated with the liver or other viscus.

"Advise emptying the uterus."

On December 15, the uterus was emptied by laparotomy, the operation being completed in thirty minutes. At first there seemed to be improvement, but the patient died three days later without any postoperative complications, and continuing in the course of her previous condition.

Autopsy Report.—The following positive findings are quoted from the autopsy report:

"The calvarium, dura, falx, and tentorium are normal. Fluid blood in all venous sinuses. There is a moderate increase in the amount of clear fluid in the subarachnoid space and the basal cisterns. The vessels over the cortex are markedly congested and there are occasional small petechial hemorrhages over the cortex. The large vessels show no arteriosclerosis. There is a slight shrinking of the gyri with widening of the sulci.

"The right lung is similar to the left. Cut surface exudes a moderate amount of edema. There is an occasional small patch of moist consolidation. Moderate amount of cloudy, frothy fluid in bronchus.

"The left kidney measures 12 x 5 x 3½ centimeters. Capsule strips easily. Surface smooth, pale, and swollen. Cut surface cloudy, with occasional small hemorrhages in pelvis. Ureter normal.

"The liver is small, measures 20 x 14 x 8 centimeters. Surface smooth. Cut surfaces rather markedly congested and brown; no hemorrhages.

"The right kidney measures 12 x 4½ x 3¼ centimeters, and is similar to the left, pale, edematous and cloudy. The pelvis is moderately dilated, and the ureter is dilated to about twice the normal size. There is no obstruction of the right ureter to the passage of a probe."

Microscopic Examination

Kidney.—Slight cloudy swelling of convoluted tubular epithelium, slight amount of coagulated albumen in occasional glomerular capsular space, few hyalin casts. Otherwise, the renal tissue is normal.

Liver.—Slight, cloudy swelling, granular and fatty degeneration and necrosis of the central liver cells; but the liver is practically normal.

Lungs.—1. Patches of air-bearing alveoli, and large collections of alveoli filled with inflammatory exudate, chiefly polymorphonuclears, edema, and a few red cells. Bronchioles filled with purulent exudate.

2. Chiefly normal air-bearing lung with scattered areas of edema.

Brain (Left Cerebral Cortex).—The meningeal vessels are moderately congested, polymorphonuclears prominent among the red cells. Moderate numbers of red cells free in the subarachnoid space in areas. Small hemorrhages are scattered through the cortex, with slight central necrosis.

Left Wall of Third Ventricle.—The white matter beneath the ependyma contains many perivascular hemorrhages of different ages, some composed entirely of intact red cells, others showing tissue necrosis.

White Matter Left Cerebral Hemisphere.—Normal other than rather marked congestion of blood vessels. No hemorrhages.

Sections of the Brain After Hardening.—Show the ventricles normal in size. Many dilated blood vessels throughout the white matter, with small hemorrhages in the gray matter in areas. The walls of the third ventricle and extending out into the white matter for one centimeter are hemorrhagic. The remainder of the brain appears normal grossly.

Bacteriologic Examination.—Smear.

Lung.—Right: Many polymorphonuclears, many Gram-positive diplococci, many intracellular.

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Doctor Gerstle (Closing).*—We are thoroughly in accord with Doctor Eaton when he states that there exists no absolute proof of the pathogenesis of the condition under discussion. However, until such a time as more detailed and accurate knowledge is available, we feel very strongly the advisability of prophylactic vitamin-rich diets.

The extremely interesting case presented by Doctor Schaupp is of particular value due to the detailed necropsy report. It is regrettable that, apparently, it was not feasible to examine the spinal cord and peripheral nerves; but inasmuch as necropsy findings in this condition have been rarely reported, Doctor Schaupp's case is of special value.

* Since this paper has been completed, an excellent article on the same subject, entitled "Gestational Polyneuritis," by Drs. E. D. Plass and W. F. Mengert, has appeared in *The Journal of the American Medical Association* (Dec. 23, 1933, Vol. 101, No. 26).